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CYTOGENIC EFFECT OF IONIZING RADIATION AND STREPTOMYCIN

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In the report (Reference 1), it was indicated that during the action of streptomycin upon cells' nuclei, at high concentrations it emerges as a mutagenic factor, while at low concentrations it proves antimutagenic, suppressing the natural mutagenic process. In the present report, we present data concerning the cytogenetic effect of the combined action of ionizing radiation with streptomycin. Considering the complex nature of streptomycin's effect upon the metabolism processes (References 2-4) occurring in a cell, we made an evaluation of its interaction with radiation at various phases of the cellular cycle.

In the test series, small roots of onions were processed in a streptomycin solution at a concentration of $5 \cdot 10^{-3}$ mm and were exposed to gamma rays (250 r) or by neutrons (30 rad). To evaluate the effect of radiation on various phases of the fission cycle, small roots of an onion (without introduction of streptomycin) were examined at various times after exposure.

The fission cycle in the onion takes 20 hours, and the duration of the actual mitosis amounts to 2.5 hours (Reference 5). During radiation, the duration of fission is evidently close to 24 hours. The data in Table 1 indicate that the maximum sensitivity is inherent to the prophase (2.4 hours) and evidently to the late interphase (9 hours). The minimum ratio sensitivity typifies the middle and early interphase (16, 29 and 24 hours). Data are also given in Table 1 on the sensitivity of the same phases of fission, but at processing of the roots by streptomycin for 2 hours and for 1 hour before exposure. We observe that in the first hours after exposure, i. e. during exposure of the late interphase and prophase, the number of chromosome reconstructions decreases considerably. We are confronted by the protective effect of streptomycin, equalling 51% as a whole. For the middle and late interphases, there is no protective effect.

The data derived also show that at introduction of streptomycin at stages following the exposure, there is no perceptible additional delay of fission -- the radiation effect in these conditions, at fixation of the material after 16, 20, and 24 hours, proved the same as in the test. This pattern would have been different in case of a phase displacement of the cellular cycle.

As a result, at a conventional analysis (after 24 hours), one can conclude that the processing by streptomycin before exposure does not have a protective effect. In this case, its effect transfers to the late interphase and to the prophase.

Upon introduction of streptomycin prior to exposure, it remains unclear whether it takes effect, at the moment of exposure, upon the primary mechanisms at the evoking of mutations, or whether its effect occurred after exposure, when the potentially altered chromosomes enter the cellular cycle at the stage sensitive to streptomycin.

In infusoria (References 6, 7) and in mice (Reference 8), there was demonstrated the protective effect of streptomycin upon its introduction after exposure. We conducted a new analysis of this question by way of investigating the effect of streptomycin at all phases of the cellular cycle after exposure. For this purpose, we processed onion rootlets at various times after exposure, by using a streptomycin solution and hardening (fixing) them after 24 hours had elapsed following exposure. By such a method, we traced the development of the exposed early interphase in case of effect of streptomycin upon the various stages of the cellular cycle.

In a controlled test, with the introduction of streptomycin, we obtained 20.9% of cells with chromosome reconstructions (See Table 2). At introduction of streptomycin, the pattern changed abruptly. On one hand, upon its introduction, in 2 and 4 hours, the number of chromosome reconstructions decreased perceptibly (12.7% and 10.0%), and the protection amounted to about 48%. On the other hand, at processing after 9, 12 and 16 hours, there is a notable increase in the number of chromosome reconstructions (38.4, 30.0, 30.7%). Basically the same pattern was also established during the action of fast neutrons with the introduction of streptomycin after exposure. The difference consists in that a distinct protection is manifested only in case of the introduction of streptomycin in 2 hours after exposure and that there is a more stable increase in the number of aberrations at introduction of streptomycin in 4, 9, 16, 18 and 20 hours following exposure (Table 2).

Both the protective as well as the sensitizing effect of streptomycin was revealed in this test. Exerting an effect upon the potential changes originating in the early interphase, streptomycin protected the chromosomes from them during the first 4 hours following exposure. On the other hand, upon introduction after 9 hours, its effect led to an intensification of the radiation damage. During the action of the neutrons, this transition from a protective effect to a sensitizing one was accomplished even sooner and more clearly.

At introduction of streptomycin after exposure, its protective effect passes to the early interphase, while the sensitizing effect passes to the late interphase and the prophase (Table 2). On the other hand, its introduction before exposure evokes protection in the late interphase and prophase, and therein the sensitizing effect is not revealed in the remaining phases of the cellular cycle (Table 1). Evidently an explanation of these facts points to the fact that the protective effect of streptomycin is not connected with the stage of the cellular cycle, but with the life period of the potential changes in the chromosomes. Protection is possible only in the periods relatively close to exposure, i. e. up to the time of the appearance of the changes in the chromosomes. The duration of the potential changes should be recognized as long. This is evident from the fact that, by disrupting the processes of natural restoration of the original structures, in potentially modified chromosomes, after 9, 12, 16 and 20 hours following exposure, the streptomycin assumes the role of a factor sensitizing the radiation damage. The absence of such a sensitizing action in the tests during the introduction of streptomycin before exposure is evidently connected with the circumstance that in this case streptomycin exerted a protective effect in the first periods after exposure, but later, it exerted a sensitizing effect. As a result, quantities of chromosome reconstructions were derived which were similar to the test quantities.

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TABLE 1

1) Цитогенетический эффект гамма-лучей при их действии на различные фазы клеточного цикла без обработки и с обработкой стрептомицином до облучения

	2) Сроки фиксации после облучения (в часах)											
	3) без обработки						4) с обработкой стрептомицином					
	4	6	9	16	20	24	4	6	9	16	20	24
5) Всего изучено клеток	501	482	481	416	572	482	509	613	534	767	870	1057
6) Число клеток с хромосомными перестройками	244	230	292	143	155	95	110	146	187	261	197	201
7) Число измененных клеток (в %)	48,7±2,2	47,7±2,2	60,7±2,2	34,4±2,3	27,1±1,8	19,7±1,8	21,6±1,8	23,8±1,7	35,0±2,0	34,1±1,7	22,7±1,4	19,0±1,2

1. Cytogenetic effect of gamma rays during their effect upon various phases of the cell cycle without processing and with processing by streptomycin before exposure.

2. Periods of fixation after exposure (in hours).

3. Without processing.

4. With processing by streptomycin.

5. Total cells studied.

6. No. of cells with chromosome reconstructions.

7. No. of modified cells (in %).

TABLE 2

1) Цитогенетический эффект гамма-лучей и быстрых нейтронов при обработке стрептомицином корешков лука в разные сроки после облучения

	2) Сроки обработки стрептомицином после облучения (в часах)														
	3) воздействие гамма-лучами								4) воздействие нейтронами						
	5) контроль без стрептомицина	2	4	6	9	12	16	20	6) контоль без стрептомицина	2	4	9	16	18	20
7) Всего изучено клеток	1627	1149	1154	857	925	648	499	801	344	840	305	308	549	127	468
8) Число клеток с хромосомными перестройками	340	146	115	172	255	194	153	225	87	144	103	150	226	52	188
9) Число измененных клеток (в %)	20,9±1,0	12,7±0,9	10,0±0,8	20,1±1,3	38,5±1,5	30,0±2,0	30,7±1,8	25,0±1,5	25,3±1,0	17,1±1,2	33,8±2,7	48,7±2,8	41,2±2,1	40,9±4,3	40,2±2,2

1. Cytogenetic effect of gamma rays and of fast neutrons during processing (by streptomycin) of onion rootlets at various times after exposure.

2. Times of processing by streptomycin after exposure (in hours).

3. Effect of gamma rays.

4. Effect of neutrons.

5. Test without streptomycin.

6. Test without streptomycin.

7. Total cells studied.

8. No. of cells with chromosome reconstructions.

9. No. of modified cells (in %).